

Entrusted to operate the C.W. Bill Young Cell Transplantation Program

#### **National Coordinating Center**

3001 Broadway St. N.E. Suite 500 Minneapolis, MN 55413-1753

> Toll Free: 1 (800) 526-7809 Phone: (612) 627-5800 www.marrow.org

#### **Board of Directors**

Robert D. Lorentz, Ph.D. - Chair Edward L. Snyder, M.D. - Vice Chair Rebecca A. Lewis, Esq. - Secretary Edgar Milford, M.D. - Past Chair Daniel D. Arndt Laurence D. Atlas, Esq. Thomas K. Berg, Esq. Eugene Boyd Theresa M. Boyd, M.D. Arthur W. Bracey, M.D. Jennifer A. Christian Airam da Silva, M.P.H. Stella Davies, M.B. B.S., Ph.D., M.R.C.P. Andrea Feldmar Jacquelyn Fredrick Sergio A. Giralt, M.D. Russell J. Hammer Robert Howard Dave Huddleston Naynesh R. Kamani, M.D. Susan F. Leitman, M.D. Mary Faith Marshall, Ph.D. Rebecca McCullough Adam C. McFadden Esperanza B. Papadopoulos, M.D. Thomas H. Price, M.D.

> Jeffrey W. Chell, M.D. Chief Executive Officer

Randal K. Wada, M.D. John P. Whiteley

John R. Wingard, M.D.

Robert A. Rivera

Susan L. Rossmann, M.D., Ph.D.

February 05, 2008

Commander Russell Shilling, USN Program Officer, Medical Services Corps Office of Naval Research (ONR 341) 875 N. Randolph St. Arlington, VA 22203

Subject: Quarterly Performance/Technical Report of the National

Marrow Donor Program<sup>®</sup>

Reference: Grant Award #N00014-06-1-0704 between the Office of Naval

Research and the National Marrow Donor Program

Dear Commander Shilling:

Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of October 1, 2007 to December 31, 2007.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Medical Officer – Dennis L Confer, MD directly at 612-362-3425.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation. Other such quarterly documentation has been previously submitted under separate cover.

Please direct any questions pertaining to the cooperative agreement to my attention (612-362-3403 or at cabler@nmdp.org).

Sincerely,

Carla Abler-Enickson

Carla Abler-Erickson, MA Sr. Contracts Representative

Enclosure: One (1) copy of SF298

C: R. Baerga – ACO (ONR-Chicago), letter and enclosure Dr. Robert J. Hartzman, CAPT, MC, USN (Ret): letter and enclosure DTIC (Ste 0944): letter and enclosure NRL (Code 5227): letter and enclosure Dennis Confer, MD, Chief Medical Officer, NMDP, letter only Michelle Setterholm, NMDP letter only

#### NATIONAL MARROW DONOR PROGRAM®

Creating Connections. Saving Lives.™

#### Grant Award N00014-06-1-0704

# QUARTERLY PERFORMANCE / TECHNICAL REPORT FOR OCTOBER 1, 2007 to DECEMBER 31, 2007

Office of Naval Research

And

The National Marrow Donor Program 3001 Broadway Street N.E.
Minneapolis, MN 55413
1-800-526-7809

#### QUARTER PROGRESS REPORT

TABLE OF CONTENTS				
TASK	DESCRIPTION STATUS			
IIA	Contingency Preparedness			
IIA.1	Hypothesis 1 – Care Plans by Transplant Physicians			
IIA.1.1	Aim 1 – Secure Interest of Transplant Physicians	Open	4	
IIA.1.2	Aim 2 – GCSF in Radiation Exposure	No Activity	4	
IIA.1.3	Aim 3 – Systems to Support a Contingency Event	Open	4	
IIA.1.4	Aim 4 – National Data Collection Model	No Activity	6	
IIA.2	<b>Hypothesis 2 – Coordination of Care of Casualties</b>		6	
IIA.2.1	Aim 1 – Contingency Response Network	Open	6	
IIA.2.2	Aim 2 – Standard Operating Procedures	No Activity	8	
IIA.3	Hypothesis 3 – Information Technology Infrastructure		8	
IIA.3.1	Aim 1 – I.S. Disaster Recovery	Open	8	
II.B	Rapid Identification of Matched Donors		9	
II.B.1	Hypothesis 1 – Resolution of Speeds Donor Selection			
IIB.1.1	Aim 1 – Increase Registry Diversity	Open	9	
IIB.1.2	Aim 2 – Evaluate HLA-DRB1 High Resolution Typing	Closed	9	
IIB.1.3	Aim 3 – Evaluate HLA-C Typing of Donors	Closed	9	
IIB.1.4	Aim 4 – Evaluate Buccal Swabs	Open	10	
IIB.1.5	Aim 5 – Enhancing HLA Data for Selected Donors	Open	10	
IIB.2	Hypothesis 2 – Improve HLA Quality & Resolution		11	
IIB.2.1	Aim 1 – Collection of Primary Data	Open	11	
IIB.2.2	Aim 2 – Validation of Logic of Primary Data	Closed	11	
IIB.2.3	Aim 3 – Reinterpretation of Primary Data	Closed	11	
IIB.2.4	Aim 4 – Genotype Lists & Matching Algorithm	No Activity	11	
IIB.3	Hypothesis 3 – Algorithm to Predict Best Donor		12	
IIB.3.1	Aim 1 – Phase I of EM Haplotype Logic	Open	12	
IIB.3.2	Aim 2 – Enhancement of EM Algorithm	Open	12	
IIB.3.3	Aim 3 – Optimal Registry Size Analysis	Open	12	
IIB.3.4	Aim 4 – Target Underrepresented Phenotypes	Open	13	
IIB.3.5	Aim 5 – Bioinformatics Web Site	Open	13	
IIB.3.6	Aim 6 – Consultants to Improve Algorithm	Open	13	

IIB.4	Hypothesis 4 – Reduction of Donor Matching Time			
IIB.4.1	Aim 1 – Expand Network Communications Open			
IIB.4.2	Aim 2 – Central Contingency Management	Open	15	
IIC.	Immunogenetic Studies		15	
IIC.1	Hypothesis 1 – Influence of HLA Mismatches		15	
IIC.1.1	Aim 1 – Donor Recipient Pair Project	Open	15	
IIC.2	Hypothesis 1 – Role of Other Loci and GVHD			
IIC.2.1	Aim 1 – Analysis of Non-HLA Loci Open			
IIC.2.2	Aim 2 – Related Pairs Research Repository Open			
IID	Clinical Research in Transplantation			
IID.1	Hypothesis 1 – Clinical Research Improves Outcomes			
IID.1.1	Aim 1 – Observational Research, Clinical Trials and NIH Transplant Center Open			
IID 1.2	Aim 2 – Research with NMDP Donors Open			
IID.1.3	Aim 3 – Expand Immunobiology Research Open			
	Acronym List		19	

	y Preparedness – Hypothesis 1: Recovery of casualties with significant myelosuppression following radiation or re is optimal when care plans are designed and implemented by transplant physicians		
IIA.1.1 Aim 1:	The NMDP works to educate physicians and their medical staff as well as to disseminate information		
Secure Interest	about its contingency planning through this AIM.		
of Transplant			
Physicians	Period 5 Activity:		
	<ul> <li>Graded 335 BRT exams submitted by RITN centers; total submitted BRT exams is now 742</li> </ul>		
	Developed and implemented a Web based submission interface for the BRT exams		
	Transferred the BRT materials into presentation format to facilitate training of groups		
	<ul> <li>Collated all presentation slides from RITN conference in Sept. into one document for RITN center staff reference and posted on RITN website</li> </ul>		
	<ul> <li>Procured www.RITN.net and <u>www.RITN.org</u></li> </ul>		
IIA.1.2 Aim 2: GCSF in Radiation Exposure	This AIM focuses on non-transplant treatment guidelines and patient assessment related to the use of GCSF for patient treatment as a result of radiation exposure.  Period 5 Activity:  No Activity this period		
IIA.1 3 Aim 3: Systems to	This AIM focuses on transplant treatment guidelines; including the refinement of guidelines for patient assessment, product selection and transplant in radiation exposure situations.		
Support a Contingency	Period 5 Activity:		
Commigency	Cord blood bank recruitment registered 4,060 new cords and made them available for search. Cord blood bank conversion mapping continues with New York Blood Center. The new banks Sheba (Israel) and Gift of Life have completed conversions and are in the process of user acceptance testing.		
	To support our quality efforts, the following changes were made to CORD Link Web:		
	<ul> <li>E-Workup form was implemented and is currently in Beta test</li> <li>Medical form Maternal Risk Questionnaire and Family Medical History Questionnaire changed to support</li> </ul>		

#### Development of Medical Technology for Contingency Response to Marrow Toxic Agents October 01, 2007 through December 31, 2007

#### "Chagas EIA" and "RIPA" Confirmatory tests

- Recipient diagnosis and remission history detail was added to the order request
- Cord Blood Unit Delivery form changed

#### Additional CORD Link Web features added:

- Online query request in CORD Link Web. These requests are automatically added to NMDP"s request system for developer assignment
- CORD Link Query support for NCBI
- Funding Tools for cord banks to allow them to manage funding assignment and tracking.
- XML transactions are in Beta test which will allow for faster integration of data with the enterprise systems.

#### CRIS Link:

In the last quarter of 2007, CRISLink was updated to allow repository staff to store Local ID's, along with the assigned NMDP ID's, for samples that are received with Local ID information. This enhancement was implemented specifically to allow the Gift of Life registry to send the NMDP samples directly from donor drives where only the Gift of Life ID has been attached. The repository staff labels these samples with NMDP ID's and enters both Local and NMDP ID's into CRISLink. CRISLink communicates the association of the Local ID with the NMDP ID back to the Donor Center, and communicates the NMDP ID forward into the rest of the NMDP's systems for donor selection, typing, registration, etc. This update was successfully deployed, and now awaits full usage by the Gift of Life Registry.

#### Research Sample Repository:

The Related Pair Repository functionality was released to the Research Repository in the last quarter of 2007. This functionality allows the repository to help track TC participation with the SCTOD. The software allows the repository staff to assign and send labels to participating TCs. These TCs use the labels to assign IDs to non-NMDP facilitated related donor transplants. Samples from the recipient and donor involved in these transplants are subsequently sent to the Research Repository, where they are recognized as related pair samples, stored and made available for research studies.

#### Development of Medical Technology for Contingency Response to Marrow Toxic Agents October 01, 2007 through December 31, 2007

#### IIA 1.4 Aim 4: National Data Collection Model

The focus of this AIM is to define and develop a national data collection and management model to collect data from a mass radiological exposure event.

#### **Period 5 Activity:**

• No activity this period

**IIA.** Contingency Preparedness – Hypothesis 2: Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.

#### IIA.2.1 Aim 1: Contingency Response Network

Efforts related to this AIM are focused on the develop the Radiation Injury Treatment Network (RITN), a permanent organization of transplant centers, donor centers and cord blood banks to maintain a contingency response network.

#### **Period 5 Activity:**

#### **Exercises:**

- Conducted a setup drill of the NMDP emergency operations center to verify our ability to setup a functional operations center. During this drill we verified telephone functionality, computer connectivity and the WebEOC connection (Internet based crisis management system)
- Developed WebEOC online reports to communicate critical information to the Network as well as for the Network to communicate with the NMDP
- Created a WebEOC basic user manual
- Received RITN tabletop exercise results from all RITN centers
- Participated in the federal exercise TOPOFF 4
  - o TOPOFF 4 involved a scenario where dirty bombs were detonated in Guam, Portland and Phoenix
  - Our participation included the activation of the NMDP emergency operations center as well as activating a portion of RITN and coordinating with HHS-ASPR
  - o RITN centers communicated through the WebEOC interface including the submission of a

#### Development of Medical Technology for Contingency Response to Marrow Toxic Agents October 01, 2007 through December 31, 2007

capabilities report as part of the exercise

o Conducted an After Action Review (AAR) which documented improvements to processes for future incidents and exercises

#### **Meetings:**

- Attended the annual planning meeting of the AABB Inter-organizational Task Force on Domestic Disasters and Acts of Terrorism
- Initiated the creation of an MOU between RITN and AABB
- Held three (3) conference calls with RITN centers to assist in completion of milestones and to improve integration into the network.
- Attended and completed DHS-ODP conducted training classes:
  - o WMD Radiological/Nuclear Awareness Train-the-Trainer (AWR141)
  - o WMD Radiological/Nuclear Responder Operations (PER240)
- Attended M-STEP; conference included nuclear threat briefing by FBI Assistant Director for Counter Terrorism
- Presented general preparedness information at Council Meeting to NMDP Network
- Held RITN meeting at Fall Council

#### **Communications:**

- Distributed additional satellite telephones; a total of 60 phones are distributed to RITN centers
- Procured dedicated telephones and telephone lines for use in the EOC, this will allow us to publish a standard phone list for use during an emergency and setup for operation significantly faster
- Temporarily issued a satellite telephone to a donor center and cord blood bank in San Diego as a backup communication option due to southern California wild fires
- Distributed additional GETS cards; a total of 127 cards are issued to NMDP staff and RITN centers
- Conducted communication tests with the NMDP Network (November), a GETS card user test (November), and a satellite telephone test (November)

#### **RITN development:**

- Reviewed submitted RITN center standard operating procedures
- Completed the signing of 53 centers to participate in RITN:
  - o 37 transplant centers

	<ul> <li>9 donor centers</li> <li>7 cord blood banks</li> </ul>				
IIA.2.2 Aim 2:	This AIMs goal is to develop and test standard operating procedures, in conjunction with core transplant				
Sibling Typing	centers, to manage the activities required to HLA type siblings of casualties to evaluate their potential as				
Standard	HSC donors for their affected family member.				
Operating					
Procedures	Period 5 Activity:				
	No activity this period				
	y <b>Preparedness</b> – <b>Hypothesis 3:</b> NMDP's critical information technology infrastructure must remain operational by situations that directly affect the Coordinating Center.				
<b>IIA.3.1 Aim 1:</b>	The focus of this AIM is to ensure NMDP's ability to access and utilize its information management and				
I.S. Disaster	communication infrastructure in a contingency situation in which its Minneapolis Coordinating Center is				
Recovery	damaged or destroyed.				
	Period 5 Activity:				
	Business Continuity Planning:				
	o CSRS development:				
	<ul> <li>Conducted cost analysis for VPN based staff recovery option</li> </ul>				
	<ul> <li>Developed draft flow chart of NMDPs possible response processes related to incidents</li> </ul>				
	resulting in the inaccessibility of the Coordinating Center by staff				
	o Shelter in place materials and instructions installed at Repository				
	<ul> <li>Secured two satellite telephones at Repository</li> </ul>				
	o Coordinated with Fire Marshall to conduct fire extinguisher training at Repository				
	<ul> <li>Procured weather radios for Coordinating Center Reception and the Repository</li> </ul>				
	• <b>Disaster Recovery Planning:</b> there were no significant modifications or changes to the Disaster Recovery Site during this time. Only routine maintenance was performed.				

volunteers on the registry will speed donor selection.			
Period 5 Activity:			
recruited donors.			
quirement of ≤1.5% of typing results			
igning up for the			
The NMDP Center Support Services group will perform all donor form entry activities in 2008. To support the increased workload, the STAR Link Web Pending Donor Workflow Management screens were updated allowing the CSS group to organize donor follow up and error correction forms.			
Additional STAR Link features added in this period were:			
l c			

#### Development of Medical Technology for Contingency Response to Marrow Toxic Agents October 01, 2007 through December 31, 2007

#### **IIB.1.4 Aim 4:**

#### Evaluate Buccal Swabs

#### **Period 5 Activity:**

In April of 2006, the NMDP transitioned to the use of buccal swabs for the collection of DNA samples from newly recruited donors. To support this change in sample type, Quality Control samples for donor recruitment HLA typing also had to be changed to swab samples.

Alternative cell types chosen for blind Quality Control swab samples continued to be evaluated.

- Swabs dipped into B-Lymphocytic Cell Line (B-LCL) cultures replaced DNA dipped swabs and "Real" buccal swabs
- 27 B-LCL cell lines were used for swab creation. Vials of cells from approximately 200 additional unique cell lines are currently available for swab creation.

In September, 2007, a Sample Storage Research Study was initiated to determine the usefulness of donor buccal swab samples, stored over time, for HLA testing.

- Samples were sent to the HLA laboratories for Time Point Zero.
- Results were received for all samples from both HLA testing laboratories. HLA results were 100% accurate, and DNA quality was excellent for all samples.
- B-LCL swabs from 10 unique cell lines were sent to both HLA testing laboratories for the QC portion of the Sample Storage Research Study. Results have been received from one laboratory. HLA results were accurate.
- The next testing time point is September, 2008.

#### **IIB 1.5 Aim 5:**

# Enhancing HLA Data for Selected Donors

#### **Period 5 Activity:**

This aim consists of two prospective, registry-based typing projects, which have the potential to strategically identify and improve the HLA typing and availability of donors most likely to match searching patients from domestic TCs.

The primary goal of the Replacement Donor Pilot Study was to identify an HLA-A, B, DRB1 identical replacement donor for every donor selected for workup by a TC.

• The six month pilot project finished in September. Final data analysis continued and a report will be

	completed next quarter.	
The primary objective of the Optimum Donor Pilot Study was to develop a systematic strategy to classify donors into phenotype categories based upon the likelihood to appear on a patient's search. Adult donors high potential to match searching patients were selected and proactively contacted to verify availability, u HLA, and/or secure additional stored samples in an effort to increase the utilization of NMDP donors and reduce the search times for patients.		
	The selected, HLA typed donors will be monitored over the next six months for patient-directed activity.	
	Minor improvements were made to the requesting process for the Optimal Donor Project. Required IT support and maintenance activity for this aim have been low.	
_	<b>tification of Matched Donors – Hypothesis 2:</b> Primary DNA typing data can be used within the registry to ty and resolution of volunteer donor HLA assignments.	
IIB 2.1 Aim 1: Period 5 Activity:		
Collection of Primary Data	A meeting to discuss data requirements with an SBT kit vendor was held. Analysis is proceeding on implications to the HML primary data reporting format for group specific sequencing primers. Development is also beginning on data interpretation for sequence data without group specific primers.	
IIB 2.2 Aim 2:	Period 5 Activity:	
Validation of Logic of	This task is closed.	
Primary Data		
IIB 2.3 Aim 3:	Period 5 Activity:	
Reinterpretation of Primary Data	This task is closed.	
IIB 2.4 Aim 4:	Period 5 Activity:	
Genotype Lists & Matching	No activity this quarter.	
Algorithm		

Development of Medical Technology for Contingency Response to Marrow Toxic Agents October 01, 2007 through December 31, 2007

**IIB. Rapid Identification of Matched Donors – Hypothesis 3:** Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.

#### **IIB.3.1** Aim 1:

#### Phase II of EM Haplotype Logic

#### **Period 5 Activity:**

The final stages of logic development for the second phase of HapLogic<sup>TM</sup> continued. HLA-C and DQB1 loci predictions were computed and analyzed on reference datasets. New A-B-DRB1 haplotype frequencies were compared to past datasets confirming improvements in A-B-DRB1 predictions. Validation included analysis of a comprehensive retrospectively generated dataset where the actual results of informative donor confirmatory typings (CT or Customized) in the Registry were compared to predictions made by HapLogic. Scientific Services and Bioinformatics staff categorized and began analysis of the data generated from the validation. Any potential questions/defects that were logged for more in depth review by Bioinformatics and Scientific Services were resolved. A final summary report of this work is expected in the next quarter.

HapLogic II is on schedule for a late January release.

#### **IIB 3.2 Aim 2:**

## Enhancement of EM Algorithm

#### **Period 5 Activity:**

The third phase of prospective high-resolution minority retyping was completed and these data were included in the high-resolution haplotype tables used for HapLogic<sup>TM</sup>. These new data, and a correction to a problem with the original data extract, were submitted to Human Immunology and accepted for publication under the title: Corrigendum to "High-resolution HLA alleles and haplotypes in the United States population".

A draft of a manuscript "Revealing the History of Jewish Populations using HLA" has been developed and an abstract submitted and accepted to the 2008 EFI annual meeting for oral presentation.

#### **IIB 3.3 Aim 3:**

#### Optimal Registry Size Analysis

#### **Period 5 Activity:**

A meeting of renowned population geneticists was held in Chicago on Dec. 3, 2007. This group addressed a set of focused discussion questions about registry size and matching models. In general the group supported the approach of using ML methods to estimate haplotype frequency and HW projection to model matching. Many issues were raised relating to population structure (HW deviation, admixture, sub-populations, small sample size) and a number of new approaches were proposed such as the use of a HWE correction parameter based on Fst. A prospective study plan was outlined by this group which will be operationalized as part of the activity on the next research grant (to be completed during calendar 2008).

IIB 3.4 Aim 4: Target Underrepresented Phenotypes	Period 5 Activity:  During the past quarter geographical data were refreshed to look at how actual recruitment in high-diversity areas compared to predictions. The US ZIP3 regions were separated into 4 quartiles based on previously observed diversity from high to low. 194,443 donors recruited since the previous analysis (2006) were then analyzed. The results showed that indeed there was more diversity (defined as donors with low phenotype count (1-10)) in the highest quartile regions. The predictions of this model can be used to identify areas of the country that contribute significantly more than others in terms of useful genetic diversity. The data demonstrate that if recruitment were to be carried out in way that focuses on these regions, the "useful" diversity provided by the same number of donors could be increased by at least 15%.
IIB 3.5 Aim 5: Bioinformatics Web Site	Period 5 Activity:  During the past quarter the HLA frequencies on the bioinformatics web site were updated to reflect the new data as described in IIB 3.2.
IIB 3.6 Aim 6: Consultants to Improve Algorithm	Period 5 Activity:  This funding on this Aim supports HLA Search Strategy Advice (SSA) for any TC that requests the free service. The SSA program uses external and internal experts to write reports summarizing a search strategy for each patient to help the TC identify the best potential stem cell source for their patient. Both internal and external experts participate in a rigorous QC program. The experts also assist in development and validation of enhancements for the HapLogic II algorithm.
	The SSA program completed 353 search strategy advice reports for patients at 85 different TCs this quarter (October - December 2007); the average turnaround time for all reviews was 3.7 business days.  The validation work of the internal experts is described in Aim 3.1.

# Development of Medical Technology for Contingency Response to Marrow Toxic Agents October 01, 2007 through December 31, 2007

**IIB. Rapid Identification of Matched Donors – Hypothesis 4:** Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.

#### **IIB.4.1 Aim 1:**

#### Period 5 Activity:

#### Expand Network Communications

SEARCH Link<sup>TM</sup> application upgrades

- October 2007: Patch for the September 2007 release. Added a missing question to the N2C cord validation protocol FMHQ. Added the result for a question to the GFC and version N2F cord validation protocol MRQ. Changed the display to follow industry set results for those tests, such as "*Positive*" results labeled as "*Reactive*" where appropriate for Maternal IDM forms
- December 2007: Implemented Electronic Workup for Cord Orders to replace the manual, cumbersome, paper-based process. Also, reduced the number of errors related to faxing the paper forms. The CBU Shipment Request form F00067 version 7.0 was incorporated into the shopping cart for online data entry and electronic transmission of the data. CBU order information has been added to the Request Detail screens improving operational efficiencies for the Search and Transplant Services department. Beta testing is currently in progress with one Cord Blood Bank, St. Louis Cord Blood Bank.

#### STAR II upgrades:

- Star II build 046 deployed 2007-10-23
  - o Changes to use new probe interpretation algorithm in HML processing
  - Minor changes to support E-Workup
- Star II build 047 deployed 2007-12-04
  - o Changes in preparation for CordLink XML migration
- Most StarLink centers migrated from using fixed width SDF transactions to XML transactions. This is a configuration change, but is significant as it will allow us more flexibility (new features without new transactions)

#### **Development of Medical Technology for Contingency Response to Marrow Toxic Agents** October 01, 2007 through December 31, 2007

#### **IIB.4.2 Aim 2:**

Management

Central

# Contingency

#### **Period 5 Activity:**

Central Contingency Management, accomplished through a service called Custom Search Support, used trained NMDP coordinating center staff to provide comprehensive donor/cord selection recommendations and patient search monitoring for TC staff. Navy funds support the expansion of the CSS service for contingency management.

During the quarter the NMDP provided education about the Custom Search Support service at the NMDP Council Meeting at both the general TC and roundtable sessions. The NMDP provided search support services and 95 patient search reviews for five TCs during the quarter. The policy to require Custom Search Support service for all patients from Non-Network TCs was implemented Nov 1, 2007. In this quarter 33 HLA search reviews were completed by the internal HLA search advisors for Non-Network TCs. Work progressed towards a process for the use of Custom Search Support for all affiliate member TC patients.

IIC. Immunogenetic Studies – Hypothesis 1: HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.

#### **IIC.1.1 Aim 1:**

#### **Donor Recipient** Pair Project

#### **Period 5 Activity:**

In 1994 A retrospective D/R Pair HLA typing project to characterize class I and class II alleles of donor/recipient paired samples from NMDP's Repository was initiated. The goals of this ongoing research project are to assay the impact of DNA-based HLA matching on unrelated donor transplant outcome, develop strategies for optimal HLA matching, evaluate the impact of matching at alternative HLA loci on transplant outcome and finally to promote the development of DNA-based high resolution HLA typing methodologies.

Sample Group 16 and 17 of the Donor Recipient Pair Project were audited and the data released for use in research studies. 977 donor recipient pairs were added bringing the total number of high resolution typed pairs to over 11,000.

- The period of performance for SG18 came to a close on December 31, 2007. SG18 consisted of 425 donor/recipient and 75 cord/recipient paired samples
- Typing of 489 new donor/recipient pairs and 11 cord/recipient pairs were contracted for SG19

#### Development of Medical Technology for Contingency Response to Marrow Toxic Agents October 01, 2007 through December 31, 2007

Ongoing IT support and maintenance of project tasks continued in this period. This included support of selection and shipment requests for sample group 19 of donor-patient pairs.

**IIC. Immunogenetic Studies – Hypothesis 2:** Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.

#### **IIC 2.1 Aim 1:**

### Analysis of non-HLA loci

#### **Period 5 Activity:**

In 2005 a pilot study to perform KIR ligand typing was launched. The primary objectives of the study were to move technology forward from the current practice of locus level typing to high resolution typing, disseminate information and protocols in an open source mechanism and develop reference lines for use in individual laboratories. The IPR database application will allow for storage and analysis of the non-HLA data collected.

- The Scientific Services and Bioinformatics departments continued to collaborate on the design and development of the IPR database application and tools to support immunogenetic testing projects
- Business requirement documents for the data review/resolution tools were completed. The technical specification documents are scheduled for completion next quarter
- Results for all presence/absence data along with the high resolution typing of 14 KIR loci (2DL1-5, 2DS1-5, 3DL1-3 and 3DS1) were completed and loaded into the IPR database and comparison and processing analysis was performed. Discrepancy and ambiguity data can now be extracted from the data base
- Discrepancy, ambiguity and no-make analysis and resolution of Phase 1, 2 and 3 KIR Typing Pilot project data continued

Two abstracts were accepted and the posters presented at the ASHI annual meeting on October 23, 2007:

- 1. Description of the data reporting format developed in collaboration with the NIH PPG group at the University of Minnesota and Stanford ("A community standard reporting format for KIR genotyping data")
- 2. Description of the high resolution sequence based typing methods used in the NMDP High Resolution KIR Typing Pilot Project in collaboration with the three contract laboratories ("Sequence-based typing of KIR genes")

#### Development of Medical Technology for Contingency Response to Marrow Toxic Agents October 01, 2007 through December 31, 2007

An abstract titled "Rethinking KIR Haplotype Analysis" was submitted and accepted for presentation at the Ki
Polymorphism Workshop, 2008 at Trinity College, Dublin, Ireland on 13-14th March, 2008.
Polymorphism Workshop, 2008 at Irinity College, Dublin, Ireland on 13-14th March, 2008.

#### **IIC 2.2 Aim 2:**

#### Related Pairs Research Repository

#### **Period 5 Activity:**

Sample collection began with the release of FormsNet 2.0 on December 3. Two samples were received, processed and accessioned into inventory during the quarter.

During the past quarter the Research Repository team continued to refine the specification for tools to facilitate the receipt, processing, storage and retrieval of the related samples. Tool programming was interrupted due to loss of the project programmer. A new programmer has been identified and tool development will resume next quarter.

**IID.** Clinical Research in Transplantation – Hypothesis 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.

#### **IID.1.1** Aim 1:

#### Observational Research, Clinical Trials and NIH Transplant Center

#### **Period 5 Activity:**

- At the December 2007 ASH meetings, 4 posters were presented by the GvHD Working Committee.
- Activity related to the BMT CTN PBSC vs Marrow trial continued with a total of 368 donor/patient pairs randomized at the end of this reporting quarter. As of December 31, 2007 there were 20 Workups in progress which is consistent with previous months.
- RCC trial continued. No change in accrual since the last reporting period. A meeting was scheduled for January with the investigators to discuss low accrual and potential closing of trial.
- Adult Double Cord trial activity during this period included activation of an additional site for a total of 4 sites open to accrual. A total of 3 patients were enrolled during this period which met the expected accrual goals.
- During the first quarter, the NMDP has facilitated customized and confirmatory typing requests for seven new NIH patients. One patient proceeded to the workup stage and received a PBSC transplant.

IID.1.2 Aim 2:	Period 5 Activity:				
Research with NMDP Donors	Staff continued to collaborate on a Donor Ethnicity study with Dr. Galen Switzer				
Timbr Bonors	<ul> <li>Staff began assessing requirements for collaborating with COG on a study where URD samples are being requested</li> </ul>				
	<ul> <li>Staff developed processes for a pilot of assuming responsibility for long-term donor follow-up</li> </ul>				
IID.1.3 Aim 3:	Period 5 Activity:				
Expand Immuno- biology	The CIBMTR IBWC met monthly during the quarter to discuss progress on ongoing research studies and review new proposals.				
Research	Three oral abstracts were presented at the ASH annual meeting				
	One manuscript was submitted and several draft manuscripts are in process				
	<ul> <li>Eight new proposals were received for review at the IBWC meeting during the 2008 BMT Tandem Meetings next quarter</li> </ul>				
	• The IBWC leadership continued collaboration with the IHWG Hematopoietic Cell Transplant Component to provide data and sample support to the upcoming 15 <sup>th</sup> International Histocompatibility Workshop.				
	Funding for CIBMTR IBWC studies:				
	<ul> <li>Funding provided to support sample genotyping for a study to evaluate single nucleotide polymorphisms in the P53 pathway and transplant outcome after matched unrelated donor HSCT</li> </ul>				
	<ul> <li>Funding provided to support sample and testing costs for a study designed to develop and test a prognostic index for survival in CML based on immune response gene polymorphism profiles</li> </ul>				
	<ul> <li>High Resolution testing of HLA-A, B, C, DRB1 and DQB1 of 102 maternal cord blood samples was completed for the project; "The Effects of Non-inherited Maternal Antigens (NIMA) in Cord Blood Transplantation" and analysis is underway</li> </ul>				

#### QUARTER PROGRESS REPORT

# Development of Medical Technology for Contingency Response to Marrow Toxic Agents October 01, 2007 through December 31, 2007

#### **ACRONYM LIST**

AABB	American Association of Blood Banks	CSS	Center for Support Services
AML	Acute Myelogenous Leukemia	CT	Confirmatory Testing
ARS	Acute Radiation Syndrome (also known as Acute	CTA	Clinical Trial Application
	Radiation Sickness)		
ASBMT	American Society for Blood and Marrow	DHS/ODP	Department of Homeland Security , Office for Domestic
	Transplantation		Preparedness
ASH	American Society of Hematology	DIY	Do it yourself
ASHI	American Society for Histocompatibility and	DKMS	Deutsche Knochenmarkspenderdatei
	Immunogenetics		
B-LCLs	B-Lymphoblastoid Cell Lines	DMSO	Dimethylsulphoxide
BMT CTN	Blood and Marrow Transplant - Clinical Trials	DNA	Deoxyribonucleic Acid
	Network		
BRT	Basic Radiation Training	D/R	Donor/Recipient
C&A	Certification and Accreditation	EBMT	European Group for Blood and Marrow Transplantation
CBMTG	Canadian Blood and Marrow Transplant Group	EFI	European Federation for Immunogenetics
CBB	Cord Blood Bank	EIA	Enzyme Immunoassay
CBC	Congressional Black Caucus	EM	Expectation Maximization
CBS	Canadian Blood Service	EMDIS	European Marrow Donor Information System
CBU	Cord Blood Unit	ECO	Emergency Operations Center
CHTC	Certified Hematopoeitic Transplant Coordinator	FBI	Federal Bureau of Investigation
CIBMTR	Center for International Blood & Marrow	FDA	Food and Drug Administration
	Transplant Research		
CLIA	Clinical Laboratory Improvement Amendment	FMHQ	Family Medical Health Questionnaire
CME	Continuing Medical Education	Fst	Fixation Index
CML	Chronic Myeloid Leukemia	GETS	Government Emergency Telecommunications Service
COG	Children's Oncology Group	GCSF	Granulocyte-Colony Stimulating Factor (also known as
			filgrastim)
CREG	Cross Reactive Groups	GFC	Grandfather C
CSRS	Critical Staff Recovery Site	GvHD	Graft vs. Host Disease

#### QUARTER PROGRESS REPORT

HHS	Health and Human Services	M-STEP	Minnesota Symposium on Terrorism and Emergency
			Preparedness
HIPAA	Health Insurance Portability and Accountability Act	MUD	Matched Unrelated Donor
HLA	Human Leukocyte Antigen	NCBI	National Cord Blood Initiative
HML	Histoimmunogenetics Markup Language	NCBM	National Conference of Black Mayors
HR	High Resolution	NIH	National Institutes of Health
HRSA	Health Resources and Services Administration	NIMA	Non-inherited maternal Antigens
HSC	Hematopoietic Stem Cell	NIMS	National Incident Management System
HSCT	Hematopoietic Stem Cell Transplant	NK	Natural Killer
HW	Hardy-Weinberg	NMDP	National Marrow Donor Program
HWE	Hardy-Weinberg Equilibrium	NRP	National Response Plan
IBWC	Immunobiology Working Committee	NST	Non-myeloablative Allogeneic Stem Cell
			Transplantation
IDM	Infectious Disease Markers	OCR/ICR	Optical Character Recognition/Intelligent Character
			Recognition
IHWG	International Histocompatibility Working Group	OIT	Office of Information Technology
IND	Investigational New Drug	OMB	Office of Management and Budget
IPR	Immunobiology Project Results	ONR	Office of Naval Research
ICRHER	International Consortium for Research on Health	PBMC	Peripheral Blood Mononuclear Cells
	Effects of Radiation		
IS	Information Services	PBSC	Peripheral Blood Stem Cell
IT	Information Technology	PCR	Polymerase Chain Reaction
IRB	Institutional Review Board	PSA	Public Service Announcement
KIR	Killer Immunoglobulin-like Receptor	QC	Quality control
NCI	National Cancer Institute	RCC	Renal Cell Carcinoma
MHC	Major Histocompatibility Complex	REAC/TS	Radiation Emergency Assistance Center/Training Site
MICA	MHC Class I-Like Molecule, Chain A	RFP	Request for Proposal
MICB	MHC Class I-Like Molecule, Chain B	RFQ	Request for Quotation
ML	Maximum Likelihood	RIPA	Radioimmunoprecipitation Assay
MOU	Memorandum of Understanding	RITN	Radiation Injury Treatment Network

N000014-06-1-0704

#### QUARTER PROGRESS REPORT

SBT	Sequence Based Typing	TNC	Total Nucleated Cell
SCTOD	Stem Cell Therapeutics Outcome Database	TOPOFF 4	Top Officials 4
SG	Sample Group	TSA	Transportation Security Agency
SSA	Search Strategy Advice	URD	Unrelated Donor
SSP	Sequence Specific Primers	VPN	Virtual Private Network
SSOP	Sequence Specific Oligonucleotide Probes	WMD	Weapons of Mass Destruction
SSRS	Sample Storage Research Study	WMDA	World Marrow Donor Association
STAR <sup>®</sup>	Search, Tracking and Registry	WU	Work-up
TC	Transplant Center	XML	Extensible Markup Language
TED	Transplant Essential Data		

#### REPORT DOCUMENTATION PAGE

Form Approved

OMB No. 0704-0188 Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching data sources gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Service, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, aperwork Reduction Project (0704-0188) Washington, DC 20503 PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS. 1. REPORT DATE (DD-MM-YYYY) 2. REPORT TYPE 3. DATES COVERED (From - To) 05-02-2008 Quarterly Oct - Dec 2007 5a. CONTRACT NUMBER 4. TITLE AND SUBTITLE Quarterly Performance / Technical Report N/A **5b. GRANT NUMBER** N00014-06-1-0704 **5c. PROGRAM ELEMENT NUMBER** N/A 5d. PROJECT NUMBER 6. AUTHOR(S) Setterholm, Michelle N/A 5e. TASK NUMBER Project 1, 2, 3, 4 5f. WORK UNIT NUMBER N/A 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) PERFORMING ORGANIZATION REPORT NUMBER National Marrow Donor Program N/A 3001 Broadway St., N.E., Ste. 500 Minneapolis, MN 55413 9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) 10. SPONSOR/MONITOR'S ACRONYM(S) ONR Office of Naval Research 875 N. Randolph St. 11. SPONSORING/MONITORING Arlington, VA 22203 **AGENCY REPORT NUMBER** N/A 12. DISTRIBUTION AVAILABILITY STATEMENT Approved for public release 13. SUPPLEMENTARY NOTES N/A 14. ABSTRACT 1. Contingency Prepardness: Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan. 2. Rapid Identification of Matched Donors: Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event. 3. Immunogenetic Studies: Increase understanding of the immunologic factors important in HSC transplantation. 4. Clinical Research in Transplantation: Create a platform that facilitates multicenter collaboration and data management. 15. SUBJECT TERMS Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes 16. SECURITY CLASSIFICATION OF: 17. LIMITATION OF 18. NUMBER 19a. NAME OF RESPONSIBLE PERSON ABSTRACT OF PAGES Dennis L. Confer, MD - Chief Medical Office Same as Report

21

a. REPORT

b. ABSTRACT

c. THIS PAGE

19b. TELEPONE NUMBER (Include area code)

612.362.3425